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| APPLICATION NO.         | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-------------------------|-------------|----------------------|---------------------|------------------|
| 10/572,678              | 11/27/2006  | Yinqui Wu            | P71172US0           | 4508             |
| 136                     | 7590        | 06/23/2009           | EXAMINER            |                  |
| JACOBSON HOLMAN PLLC    |             |                      | COUNTS, GARY W      |                  |
| 400 SEVENTH STREET N.W. |             |                      |                     |                  |
| SUITE 600               |             |                      | ART UNIT            | PAPER NUMBER     |
| WASHINGTON, DC 20004    |             |                      | 1641                |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/572,678             | WU ET AL.           |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | GARY W. COUNTS         | 1641                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 27 March 2009.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-31 is/are pending in the application.  
 4a) Of the above claim(s) 1-3 and 5-18 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 4 and 19-31 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date 01/07/08.

4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_.  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of Group II, claims 4 and 19-31 in the reply filed on 03/27/09 is acknowledged.
- 2.

### **Status of the claims**

3. Currently, claims 1-31 are pending. Claims 1-3, and 5-18 are withdrawn as being directed to non-elected inventions. Claims 4 and 19-31 are under examination.

### ***Specification***

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
6. Claims 4 and 19-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is vague and indefinite because the claim does not make clear the relationships that exist between the recited components of the method. For example, the preamble of the claim recites detecting hapten in a sample. However, the body of the claim recites sample analytes. It is unclear if the sample analytes are the hapten to be detected. Also, it is unclear if the antibodies recited in step (b) are the detecting molecules or if the mixture comprises both detecting molecules and antibodies. Further, the claim does not make clear if the antibodies are specific for or bind to the sample analytes or to some other component. Method claims should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. Method claims should also clearly state each component used in the method and the relationship of the various components and should not be a mere cataloging of parts. The claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

Claim 4, step (a) the recitation "the hapten molecule" there is insufficient antecedent basis for this limitation.

Claim 4, step (c) the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 4, step (d) is ambiguous in reciting, "further binding enhancement performed by flowing-through onto the surface with" because it is unclear how the instant claim is a method step. Claim 4 step d) appears to recite how certain components are intended to

be used; however, step d) does not appear to recite a positive active method step.

Accordingly, claim 4 is indefinite in being rendered incomplete.

Claim 4, step (d) the recitation "binding partner" renders the claim indefinite because it is unclear what applicant is referring to. There is insufficient antecedent support for binding partner and it is unclear what applicant intends. For example, is the binding partner referring to the detecting molecule, the antibody, the moiety or something else? Please clarify.

Claim 4 the recitations "high molecular weight" and "high mass signal" are vague and indefinite because the term "high" is a relative term which renders the claim indefinite. There is no definition provided for the phrases in the specification and therefore it is unclear what is considered to be "high molecular weight" and "high mass signal".

Claim 22 is indefinite in reciting improper Markush language in reciting, "the binding partner is selected from" because it appears to intend to limit the scope of the binding partners recited in the claims but improperly defines it as such. Perhaps, Applicant intends, "the binding partner is selected from the group consisting of."

Claim 23 the recitation "the hapten" is vague and indefinite because it is unclear if applicant is referring to the hapten recited in the preamble, which appears to be the molecule to be detected, the hapten derivative which is immobilized to the surface or the hapten molecule. See also deficiency found in claim 27.

Claim 26 is indefinite in reciting improper Markush language in reciting, "the first and second linker are independently selected from" because it appears to intend to limit

the scope of the first and second linkers recited in the claims but improperly defines it as such. Perhaps, Applicant intends, “the first linker and the second linker are independently selected from the group consisting of.”

Claim 28 the recitation “the signaler” there is insufficient antecedent basis for this limitation. See also deficiency found in claim 29.

Claim 31 is vague and indefinite because it is unclear if the analyte in claim 31 is the hapten recited in the preamble of claim 4 or if applicant intends something else.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Note: with respect to the “large protein” as recited in the claims. Since applicant has provided a definition for hapten as a small molecule of a molecular weight less than 5000 daltons. The examiner interprets large protein to be any protein greater than 5000 daltons.

10. Claims 4, 19-29 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al., (WO 02/092631) in view of Nathan et al (US 6,579,721) and further in view of Porter et al (US 2005/0089901).

Cook et al disclose rapid immunoassays for the detection of haptens in a sample. Cook et al disclose providing an immobilized hapten-linker-large group conjugate and flowing a mixture of sample hapten and antibody ligand (detecting molecule) over the immobilized hapten (e.g. pgs 18-19). Cook et al disclose that the hapten can be a derivative or progesterone (e.g. p. 9). Cook et al also disclose that there is excess ligand in the mixture (e.g. p. 37). Cook et al disclose that the method can be an immunoassay performed by surface plasmon resonance (SPR) for progesterone (pgs 18-19 and 28). Cook et al also disclose detecting the amount of antibody (binding partner) bound to the conjugate and also teach the establishment of a standard curve for determining the amounts. The linker of the conjugate comprises a chain between 10

and 50 carbon atoms in length (p. 10). Cook et al discloses that this chain can be a carbon-based chain (p. 10). The linker can also be a polyethylene glycol chain (p. 30). Cook et al also disclose that the linker can be bound to the 4-position of the A-ring structure (p. 15). Cook et al specifically disclose that an immunogold signaler can be used in the method (p. 19).

Cook et al differ from the instant invention in failing to teach a bio-conjugate for signal enhancement.

Nathan et al disclose methods and reagents for the enhancement of SPR-based detection assays. Nathan et al disclose antibodies attached to gold nanoparticles and disclose contacting a reagent of these nanoparticles into a SPR biosensor for an amplified change in signal (e.g. abstract, col 3 – col 4). Nathan et al further disclose that these nanoparticles can be exploited in any assay that depends on the occurrence of a molecular recognition event (col 3, lines 40-46, col 13, lines 40-55). Natan et al provide that methods for attaching biomolecules to metal nanoparticles are well known in the art (col 3, lines 58-61). Natan et al provide application of the nanoparticles in SPR assays leads to a 100,000 fold increase in SPR sensitivity (col 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate nanoparticle conjugates specific for the detection molecules of Cook et al because Nathan et al taught that the nanoparticles can be exploited in any assay that depends on the occurrence of a molecular recognition event and showed that the use of these nanoparticles in SPR assays leads to a 100,000 fold increase in SPR sensitivity.

Cook et al and Natan et al differ from the instant invention in failing to teach the antibody is attached to the nanoparticle by means of a linker.

Porter et al (US 2005/0089901) disclose gold nanoparticles comprising binding molecules such as antibodies. Porter et al disclose that the binding molecules are attached to the particle by linkers which can comprise 10 carbon atoms (e.g. pgs 4-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate linkers such as taught by Porter et al into the nanoparticle conjugate of Natan et al for the modified method of Cook et al because Nathan et al taught that the attachment of molecules to gold nanoparticles is very well known in the art and Porter showed that linkers are a conventional method for the attachment of biomolecules to gold nanoparticles. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating linkers such as taught by Porter et al into the nanoparticles conjugates of Natan et al for the modified method of Cook et al.

11. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al., (WO 02/092631) in view of Nathan et al (US 6,579,721) and Porter et al (US 2005/0089901) as applied to claims 4, 19-29 and 30 above, and further in view of Wu et al (Steroids 67 (2002) 565-572).

See above for the teachings of Cook et al., Nathan et al. and Porter et al.

Cook et al., Nathan et al., and Porter et al differ from the instant invention in failing to teach removing detecting molecules to regenerate.

Wu et al teaches that it is known in the art to provide solutions to the biosensor surface to remove molecules to provide for regeneration of the surface (e.g. p. 568).

It would have been obvious to one of ordinary skill in the art to incorporate regeneration techniques such as taught by Wu et al into the modified method of Cook et al because Wu et al showed that this provides for regeneration of biosensor surfaces for the reuse of the surface.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/  
Examiner, Art Unit 1641

/GAILENE R. GABEL/  
Primary Examiner, Art Unit 1641

6/21/09